UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,588	08/20/2003	Connie Sanchez	05432/100M919-US3	5265

7278 7590 02/07/2008

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
02/07/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/644,588	SANCHEZ ET AL.	
	Examiner	Art Unit	
	Timothy E. Betton	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21,23,25,27,29,31,33,35 and 37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,25,27,29,31,33,35 and 37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' Remarks filed 27 September 2007 have been acknowledged and duly made of record.

The 112, second paragraph rejection has been withdrawn based on the submission of the required amendments made by applicants.

Applicants' argument directed to 103(a) rejection, however, has been considered but not found persuasive.

The essential elements of applicants' argument are directed to the alleged disclosure and factual evidence thereof drawn to unexpected results based on the remarkable potency of escitalopram in comparison to citalopram.

Current evidentiary documentation discloses an explanation on the alleged phenomenon of escitalopram in the justification for a higher price in comparison to citalopram:

BACKGROUND: Escitalopram is the active isomer of the antidepressant citalopram. In theory single-isomer drugs may be superior but few have been found to have clinically significant advantages. The manufacturer claims that escitalopram has more efficacy and a faster onset of effect than citalopram. The purpose of this study was to assess how far these claims are justified. METHODS: Relevant trial reports were requested from H. Lundbeck A/S and the Swedish drug regulatory authority. The trials consisted of a pooled analysis of 1,321 patients from one unpublished, one partly published and one published eight-week trial, as well as a 24-week trial with 357 patients published as a poster. The studies compared escitalopram with placebo and/or citalopram in outpatients aged or =18 years who met specified criteria for depression. The trials' quality was assessed with Moncrieff et al.'s quality assessment instrument

and the results compared with the claims from the advertisements. RESULTS: The advertising claims are not justified because they are based on secondary outcomes, non-intention-to-treat analyses and arbitrarily defined subgroups. The subgroup results are inconsistent. Methodological flaws in the trials could account for the differences found. Even if the differences claimed were real they appear too small to justify higher prices. CONCLUSIONS: On the evidence available to us the manufacturer's claims of superiority for escitalopram over citalopram are unwarranted. The Swedish and Danish drug regulatory authorities reached similar conclusions. This highlights the need for wider dissemination of national authorities' statements to other countries affected by the European Union's mutual recognition procedure (Svensson et al., Escitalopram: superior to citalopram or a chiral chimera?, [online] retrieved on 1/31/2008, (2004), retrieved from http://www.biopsychiatry.com/chiralchimera.htm).

In accordance, the instant specification contains none of the elements that are drawn to a specific hallmark standard of measure as is explained in the disclosure above. Moncrieff et al.'s quality assessment instrument was incorporated to justify the quality of the study. However, the instant specification contains nothing of the sort and is silent in reference to substantive embodiments to overcome obviousness. The nature of this type of study relies considerably on correlative data and cumulative/comparative results.

Further, applicants' disclose information drawn to the Montgomery-Asberg Depression Rating Scale but there is no data in the whole of the instant specification that justifies, supports, nor suggests that the scale was actually incorporated in order to accurately determine the inventive objective of claimed invention.

Specifically, applicants disclose an intended function for the use of MADRS, however the elements necessary to determine possession of current invention are absent. Representations of the (10) factors or prongs of assessment are also absent. For instance, scores attributed to apparent sadness, reported sadness, inner tension, reduced sleep, reduced appetite, concentration difficulties, lassitude, inability to feel, pessimistic thoughts and suicidal thoughts were not present and/or evaluated in the instant specification (Montgomery-Asberg Depression Rating Scale, (MADRS), [online] retrieved 1/31/2008, (2008), retrieved from:www.cnsforum.com).

Additionally, applicants' disclosure of several published articles supporting the surprising effect of treating severely depressed patients with escitalopram is of no consequence in the absence of any substantial disclosure in the instant specification elucidating such findings. In consideration of the said specification, the skilled artisan would not be inclined to identify a clear or adequate correlation from the instant specification in view of applicants' published supporting articles.

Thus, for the reasons which are already made of record, the 103(a) rejection is maintained over instant claims 21, 25, 27, 31-33, and 37.

Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 21, 23, 25, 27, 29, 31, 33, 35, and 37 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Patris M, et al. ("Citalopram versus fluoxetine; a double-blind, controlled, multicentre, phase III trial in patients with unipolar major depression treated in general practice," 1996 International Clin Psychopharm 11: 129-136), in view of Boegesoe et al. (US Pat. 4,943,590), and further in view of Bilski et al. (US Pat. 4,764,361).

Patris et al. teach the administration of citalopram in the treatment of patients with major depression (abstract). Patients had a score of 30 on the MADRS at the beginning of the 8-week treatment period (see Fig. 1 p. 132). The reference teaches assessment of the efficacy of treatment by measuring the MADRS score as well as by the CGI severity and improvement scale (see pp. 130 and 134).

Patris et al. do not teach escitalopram (the S-enantiomer) specifically. Boegesoe et al. teach that antidepressant drug citalopram has two enantiomers, (+)-citalopram (which is escitalopram) and (-)-citalopram, and that the entire 5-HT uptake inhibition activity resides in the (+) enantiomer (i.e. escitalopram) (see: abstract; col. 1, lines 1-28; col. 2, lines 9+). The reference also teaches separation of the two enantiomers to yield pure citalopram enantiomers (see col. 2, lines 51 - col. 7, line 25). The reference teaches, "a method for alleviating depression in a living animal body subject thereto" by

administering an effective amount of the compound or pharmaceutically acceptable salts (which is escitalopram), at dosages ranging from 0.10-100 mg and preferably 5-50 mg daily (overlapping the dosage of current claim 25). (See: abstract; col. 8 Table 1; col. 8, lines 55-66; claims 1-2 & 7-12).

While Boegesoe et al. teach pharmaceutically acceptable salts; the reference does not teach oxalate salts specifically.

Bilski et al. teach the oxalate and crystalline oxalate salts of the (S) are a form of a racemic mixture. The reference does not teach escitalopram.

It would have been obvious to one of ordinary skill in the art to use the oxalate or crystalline oxalates salt of escitalopram in the instantly claimed method of treating severe depression, having been taught by the prior art that it is known to make oxalate and crystalline oxalate salts of a racemic compound to obtain the (S) isoform and motivated by the desired to obtain the (S)/(+) isoform salt of citalopram (i.e. escitalopram), which is known to be the racemate wherein the pharmaceutical antidepressant activity resides.

Claims 21, 23, 25, 27, 29, 31, 33, 35, and 37 are rejected. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

S. Wang

SHENGJUN WANG
PRIMARY EXAMINER